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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/555,897	04/18/2006	Luigi De Ambrosi	SER-103.0 P US	4476

7590
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10/24/2008

EXAMINER

KRISHNAN, GANAPATHY

ART UNIT	PAPER NUMBER
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1623

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10/24/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/555,897	Applicant(s) DE AMBROSI ET AL.	
	Examiner Ganapathy Krishnan	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 September 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 6, 8 and 9 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 6, 8 and 9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

A Request for Continued Examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed 9/29/2008 has been entered.

The Request for Continued Examination filed 9/29/2008 has been carefully considered. The following information provided in the amendment affects the instant application:

1. Claims 4-5 and 7 have been canceled.
2. New Claims 8 and 9 have been added.
3. Claims 1-3 and 6 have been amended.
4. Remarks drawn to rejections under double patenting and 35 USC 102(b) of record and a Declaration under 37 CFR 1.132 by Luigi De Ambrosi.

Claims 1-3, 6 and 8-9 are pending in the case.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

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A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 1 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2 of U.S. Patent No. 7,091,337 ('337). Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Instant claim 1 is drawn to a process for depolymerization of a heparin comprising exposing it to a dynamic UV radiation at a particular concentration range wherein the depolymerized product has a molecular weight that is less than or equal to 50% of the original molecular weight before depolymerization.

Claim 1 of '337 is drawn to a process for depolymerization of a glycosaminoglycan via exposure of the glycosaminoglycan to radiation, which reads on UV radiation. Dependent claim 2 of '337 is drawn to the process wherein the glycosaminoglycan is heparin.

Claims 1-2 '337 differ from the instant claims in that the instant claims employ dynamic irradiation at a concentration range of 2 to 25% w/v of heparin. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made that heparin at the said concentration range could be successfully employed in the method of '337.

In determining the differences between the prior art and the claims, the question is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious. Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some

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teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art. “The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art.” *In re Kotzab*, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). In the instant case, '337 teaches performing the step applicant claims. Although the claim of '337 employs a dynamic irradiation particular concentration range of heparin, one of ordinary skill in the art would readily recognize that the scheme taught by '337 could be employed in the instant method. The use of known members starting materials in reactions to effectuate the same type of modifications taught in the prior art is not seen to render the instantly claimed method unobvious over the art. Once the general reaction has been shown to be old, the burden is on the applicant to present reason or authority for believing that a particular concentration of the starting material or the way it is irradiated would affect the basic reaction and thus alter the nature of the product or the operability of the process and thus the unobviousness of the method of producing it.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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The rejection of Claims 1-3 and 6-7 under 35 U.S.C. 102(b) as being anticipated by Balazs et al (Radiation Research, 1959, 11, 149-164; document # CA in IDS of 11/07/2005) maintained in the Final rejection mailed 4/21/2008 has been overcome by amendments to instant claims 1-3 and 6. Support is seen in the instant specification for the said amendments.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 6 and 8-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Balazs et al (Radiation Research, 1959, 11, 149-164; document # CA in IDS of 11/07/2005), of record.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

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evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Balazs et al teach the depolymerization of hyaluronic acid (glycosaminoglycan) via irradiation of the hyaluronic acid with UV radiation from a low-pressure mercury lamp (UV radiation emitted at 253nm; page 150, paragraph 4). The hyaluronic acid used as starting material had a molecular weight of 80,000 and the molecular weight of the depolymerized hyaluronic acid obtained was 19,700 (M_w less than 50% of the M_w of the starting glycosaminoglycan before irradiation; page 155, first paragraph). The irradiation of the hyaluronic acid was performed below 37°C (page 150, fifth paragraph). Balazs et al also teach that similar results were obtained on irradiating heparin with UV light (page 155, last paragraph). However, Balazs does not exemplify the depolymerization of heparin via a process using dynamic irradiation and a concentration and temperature range as instantly claimed.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to depolymerize heparin via the process as instantly claimed since an analogous process has been demonstrated for other similar glycosaminoglycans in the prior art and depolymerization results for these other glycosaminoglycans is taught to be similar using heparin in the same process. It is well within the skill level of the artisan to adjust concentrations and process temperatures as a routine optimization.

One of skill in the art would be motivated to depolymerize heparin using UV radiation as instantly claimed since Balazs (page 162, lines 29-30, 3rd full paragraph) irradiation with UV

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light produces small dialyzable fractions and hence no extensive purification such as percolation through a resin (example 5) is required. Since the depolymerization can be carried out in an aqueous solution the presence of solvent and other chemical impurities derived from depolymerizing agents are avoided.

Response to Applicants' Arguments

With respect to the obviousness-type double patenting rejection of instant claim 1 over claims 1-2 of '337 patent applicants have argued that the parameters as recited in instant claim 1 is neither taught or suggested by the subject matter of claims 1-2 of the '337 patent.

Applicants' arguments and the Declaration of Luigi de Ambrosi have been considered but are not found to be persuasive.

A dynamic irradiation process is same as a continuous process. Such parameters including the concentration range of the starting heparin are parameters that one of skill in the art would vary as a routine optimization of the process. This type of optimization is known and well within the skill level of the artisan. The material depolymerized and the use of irradiation to accomplish the same are taught in the '337 patent. The recitation in claim 1 of the '337 patent does not exclude the use of UV irradiation. Also, the term high energy radiation is not defined in the claim as being confined only to radiations such as gamma radiation.

The following response is with respect to the rejection under 35 USC 103(a) above based on the remarks of applicants rebutting 35 USC 102(b) rejection advanced earlier.

Applicants have argued that:

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1. The instant process uses a dynamic irradiation step wherein the solution to be irradiated is circulating as a thin layer in a lamp jacket and then returns to a reservoir. In contrast Balaz discloses a static process wherein the sample is irradiated in a quartz cell.

2. In contrast to the instant concentrations used Balaz teaches much lower concentrations of the starting material.

3. The cationic dye binding studies reported by Balaz suggests that a large amount of very small fragments were formed in the process of Balaz. The instant process produces fragments with molecular weight less than 1000 Da in an amount less than 6%. This is an unexpected result.

Applicants' arguments and the Declaration of Luigi de Ambrosi have been considered but are not found to be persuasive.

Balaz may not have taught or suggested the circulation of the solution to be irradiated as in the instant process. The instant process is same or similar to a continuous process. The instant claims recite that the depolymerized heparin has a molecular weight less than or equal to 50% of that of the starting heparin. According to this recitation then, a depolymerized heparin having molecular weight of 1000 Da or less is heparin that has molecular weight less than 50% of the original molecular weight. The instant claims do not limit the molecular weight to a particular cut off value as instantly claimed. One of skill in the art even if desirous of producing depolymerized heparin that has a very low percentage of low molecular weight as argued and based on the results of the dye binding studies of Balaz would be led to adjusting the process parameters in order to reduce the amount of very low molecular weight fragments. One of skill in the art will recognize from the disclosure of Balaz's process that either the duration of exposure

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to radiation should be adjusted (in the static process) or the solution to be depolymerized should be continuously removed from the source of irradiation after a certain period of time. The longer the exposure to the radiation the more the reduction would be in the molecular weight. This is a logical step in the process which one of skill in the art will recognize and hence use a continuous or in other words dynamic irradiation, step in the process of Balaz. This need not necessarily be taught or suggested by the prior art. One of skill in the art also knows that in a depolymerization process like that of Balaz and the one instantly claimed, a molecular weight distribution of the depolymerized fragments is always observed. Hence, applicants' argument that Balaz's process produces a different molecular weight distribution compared to the instant process is an expected result. One of skill in the art would expect depolymerized fragments of heparin even when using starting concentrations of heparin and process temperatures in the range as instantly claimed. Applicants' Declaration does not disclose any unexpected results in the instant process.

Conclusion

Claims 1-3, 6 and 8-9 are rejected

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ganapathy Krishnan/
Examiner, Art Unit 1623

/Shaojia Anna Jiang, Ph.D./
Supervisory Patent Examiner, Art Unit 1623